(b) contacting the viral particles produced in step (a) with an antibody preparation from the patient;

(c) contacting the viral particles and antibody preparation of step (b) with a second cell, wherein the second cell expresses a cell surface receptor to which the virus binds;

(d) measuring the amount of the detectable signal produced by the second cell in order to determine the infectivity of the viral particles; and

(e) comparing the amount of signal measured in step (d) with the amount of signal produced in the absence of the antibody preparation, wherein a reduced amount of signal measured in the presence of the antibody preparation indicates that the patient has developed an antibody response to the viral protein capable of blocking infection.

47. (New) The method of Claim 46 wherein the nucleic acid of (i) is part of the viral expression vector of (ii).

48. (New) The method of Claim 46 wherein the nucleic acid of (i) is integrated into the genome of the first cell.

49. (New) The method of Claim 46 wherein the viral vector of (ii) is integrated into the genome of the first cell.

50. (New) The method of Claim 46 wherein the nucleic acid of (i) and the viral vector of (ii) are integrated into the genome of the first cell.

51. (New) The method of claim 46 wherein the viral protein is a capsid protein.

REMARKS

Applicants have amended the Specification to indicate that the instant application is a Continuation-In-Part of Application Serial Number 09/874,475, filed June 4, 2001. This amendment is made pursuant to 37 C.F.R. § 1.115. Accordingly, Applicants respectfully request that the amendment be entered.

With this amendment Claims 1 and 38-51 are pending. The claims have been amended, without prejudice, for the purpose of more clearly defining what Applicants regard as the invention.

Claims 2-37 have been canceled, without prejudice, by the accompanying Preliminary Amendment. Applicants expressly reserve the right to prosecute the subject matter of the canceled claims in one or more timely filed divisional, continuation or continuation-in-part applications.

CONCLUSION

In view of the above amendment and remarks, the subject application is believed to be in good and proper order for allowance. Early notification to this effect is earnestly solicited.

No fee is believed due in connection with this submission. However, the Commissioner is authorized to charge any required fee or credit any overpayment to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date February 15, 2002

47,763

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Appendix A
Marked-Up Copies of the Replacement Paragraphs

Deleted material is bracketed.

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In one embodiment, drug resistance mutations were introduced into well-characterized X4 tropic (NL4-3) and R5 tropic (JRCSF) viruses. T20 susceptibility was measured using the virus entry assay **(Figure 7)**. The fold change (FC) in T-20 susceptibility for each virus was determined by dividing the IC50 of the test virus by the IC50 of the HXB2 strain of HIV-1. T-20 sensitivity of similar mutant viruses bas been reported in the scientific literature (Rimsky, et al.). In this embodiment, viruses with one mutation within the GIV motif of gp41 (DIV, GIM, SIV) were less susceptible to T20 than the wildtype virus (GIV) **[(Figure 11)]**. Viruses with two mutations within the GIV motif (DIM, SIM, DTV) were less susceptible to T20 than with one, or no mutations in the GIV motif **[(Figure 11)]**.

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In another embodiment, mutations that may confer reduced (or increased) susceptibility to the entry inhibitor are identified by sequencing the envelope genes of the sensitive and resistant viruses. The deduced amino acid sequences of the sensitive and resistant viruses are compared to identify candidate drug resistance mutations. The ability of a specific mutation to confer altered drug susceptibility is confirmed or disproved by introducing the mutation into a drug sensitive virus and measuring the susceptibility of the mutant virus in the virus entry assay. In the example represented here, a short stretch of amino acid sequences within the first heptad repeat (HR-1) of the HIV-1 gp41 transmembrane envelope protein is aligned for viruses exhibiting different T-20 susceptibilities **[(Figure 11)]**. Highlighted amino acids represent mutations known to confer reduced susceptibility to T-20.

Appendix B

Claims as Pending After Entry of the Amendments

1. A method for identifying whether a compound inhibits entry of a virus into a cell which comprises:

(a) obtaining nucleic acid encoding a viral envelope protein from a patient infected by the virus;

(b) co-transfecting into a first cell

(i) the nucleic acid of step (a), and

(ii) a viral expression vector which lacks a nucleic acid encoding an envelope protein, and which comprises an indicator nucleic acid which produces a detectable signal,

such that the first cell produces viral particles comprising the envelope protein encoded by the nucleic acid obtained from the patient;

(c) contacting the viral particles produced in step (b) with a second cell in the presence of the compound, wherein the second cell expresses a cell surface receptor to which the virus binds;

(d) measuring the amount of signal produced by the second cell in order to determine the infectivity of the viral particles; and

(e) comparing the amount of signal measured in step (d) with the amount of signal produced in the absence of the compound, wherein a reduced amount of signal measured in the presence of the compound indicates that the compound inhibits entry of the virus into the second cell.

38. (New) A method for detecting within a patient infected by HIV the development of an antibody response capable of blocking infection comprising:

(a) transfecting into a first cell

i) a nucleic acid encoding a viral envelope protein from the patient, and

ii) a viral expression vector which lacks a nucleic acid encoding an envelope protein, and which comprises an indicator nucleic acid which produces a detectable signal,

such that the first cell produces viral particles comprising the envelope protein encoded by the nucleic acid obtained from the patient;

(b) contacting the viral particles produced in step (a) with an antibody preparation from the patient;

(c) contacting the viral particles and antibody preparation of step (b) with a second cell, wherein the second cell expresses a cell surface receptor to which the virus binds;

(d) measuring the amount of the detectable signal produced by the second cell in order to determine the infectivity of the viral particles; and

(e) comparing the amount of signal measured in step (d) with the amount of signal produced in the absence of the antibody preparation, wherein a reduced amount of signal measured in the presence of the antibody preparation indicates that the patient has developed an antibody response to the viral envelope protein capable of blocking infection.

39. (New) A method for detecting within a patient infected by a virus the development of an antibody response capable of blocking infection comprising:

(a) transfecting into a first cell
   i) a nucleic acid encoding a viral protein from the patient, and
   ii) a viral expression vector which lacks a nucleic acid encoding the viral protein, and which comprises an indicator nucleic acid which produces a detectable signal,

such that the first cell produces viral particles comprising the viral protein encoded by the nucleic acid obtained from the patient;

(b) contacting the viral particles produced in step (a) with an antibody preparation from the patient;

(c) contacting the viral particles and antibody preparation of step (b) with a second cell, wherein the second cell expresses a cell surface receptor to which the virus binds;

(d) measuring the amount of the detectable signal produced by the second cell in order to determine the infectivity of the viral particles; and

(e) comparing the amount of signal measured in step (d) with the amount of signal produced in the absence of the antibody preparation, wherein a reduced amount of signal measured in the presence of the antibody preparation indicates that the patient has developed an antibody response to the viral protein capable of blocking infection.

40. (New) The method of Claim 39 wherein the viral protein is a capsid protein.

41. (New) A method for detecting within a patient infected by HIV the development of an antibody response capable of blocking infection comprising:

(a) incubating a first cell comprising
   (i) a nucleic acid encoding a viral envelope protein from the patient, and
   (ii) a viral expression vector which lacks a nucleic acid encoding an envelope protein, and which comprises an indicator nucleic acid which produces a detectable signal,

such that the first cell produces viral particles comprising the envelope protein encoded by the nucleic acid obtained from the patient;

(b) contacting the viral particles produced in step (a) with an antibody preparation from the patient;

(c) contacting the viral particles and antibody preparation of step (b) with a second cell, wherein the second cell expresses a cell surface receptor to which the virus binds;

(d) measuring the amount of the detectable signal produced by the second cell in order to determine the infectivity of the viral particles; and

(e) comparing the amount of signal measured in step (d) with the amount of signal produced in the absence of the antibody preparation, wherein a reduced amount of signal measured in the presence of the antibody preparation indicates that the patient has developed an antibody response to the viral envelope protein capable of blocking infection.

42. (New) The method of Claim 41 wherein the nucleic acid of (i) is part of the viral expression vector of (ii).

43. (New) The method of Claim 41 wherein the nucleic acid of (i) is integrated into the genome of the first cell.

44. (New) The method of Claim 41 wherein the viral vector of (ii) is integrated into the genome of the first cell.

45. (New) The method of Claim 41 wherein the nucleic acid of (i) and the viral vector of (ii) are integrated into the genome of the first cell.

46. (New) A method for detecting within a patient infected by a virus the development of an antibody response capable of blocking infection comprising:

(a) incubating a first cell comprising
  (i) a nucleic acid encoding a viral protein from the patient, and
  (ii) a viral expression vector which lacks a nucleic acid encoding the viral protein, and which comprises an indicator nucleic acid which produces a detectable signal,

  such that the first cell produces viral particles comprising the viral protein encoded by the nucleic acid obtained from the patient;

(b) contacting the viral particles produced in step (a) with an antibody preparation from the patient;

(c) contacting the viral particles and antibody preparation of step (b) with a second cell, wherein the second cell expresses a cell surface receptor to which the virus binds;

(d) measuring the amount of the detectable signal produced by the second cell in order to determine the infectivity of the viral particles; and

(e) comparing the amount of signal measured in step (d) with the amount of signal produced in the absence of the antibody preparation, wherein a reduced amount of signal measured in the presence of the antibody preparation indicates that the patient has developed an antibody response to the viral protein capable of blocking infection.

47. (New) The method of Claim 46 wherein the nucleic acid of (i) is part of the viral expression vector of (ii).

48. (New) The method of Claim 46 wherein the nucleic acid of (i) is integrated into the genome of the first cell.

49. (New) The method of Claim 46 wherein the viral vector of (ii) is integrated into the genome of the first cell.

50. (New) The method of Claim 46 wherein the nucleic acid of (i) and the viral vector of (ii) are integrated into the genome of the first cell.

51. (New) The method of claim 46 wherein the viral protein is a capsid protein.